

provement after splenectomy in an icteric type of pernicious anemia. It is interesting that in Huber's case the blood cells from the splenic vein showed no decrease in resistance. As all three patients had icterus, urobilinuria, fragility of corpuscles, and splenomegaly it is probable that these cases really belong to the class of hemolytic jaundice.

One might say in summarizing that splenectomy should be considered in all those diseases where there is evidence of increased blood destruction and that in early Banti's disease and hemolytic jaundice at least the results of splenectomy have been excellent. All such procedures, however, should be entered upon most conservatively as long as so much of the physiology of the spleen remains unknown. Though its removal is known to be compatible with life, it may yet prove to have such important detoxicating relations to infection or to digestion, that splenectomy should only be practised after most careful study and to relieve the most serious conditions.^{ss}

CULTURAL AND VACCINE RESULTS IN A CASE OF HODGKIN'S DISEASE.

BY RALPH R. MELLON, M.Sc., M.D.,

ASSISTANT PROFESSOR OF PHYSICAL DIAGNOSIS AND DIRECTOR OF THE LABORATORY
OF CLINICAL PATHOLOGY, UNIVERSITY HOMEOPATHIC HOSPITAL,
ANN ARBOR, MICHIGAN.

IN the number of the *Archives of Internal Medicine*, for August, 1913, Bunting and Yates report six cases of Hodgkin's disease, from the lymphatic glands of which they have isolated a diphtheroid organism considered by them as identical with the one described by Fraenkel and Much.¹ In 1900 the last-named authors were able to extract Gram-positive, non-acid-fast, diphtheroid bacilli from the sediment of the lymph glands which had been previously treated with antiformin, to which preparation the organism was resistant.

Negri and Miermet² were the first to report successful cultivation of this organism, isolation of which was brought about on Bordet's medium (blood-glycerin-potatoagar).

Billings and Rosenow³ have isolated the same organism from eighteen cases of Hodgkin's disease, the glands of which were

^{ss} Since the above was written, numerous reports of splenectomy for pernicious anemia have appeared. Though the patient's general condition was improved temporarily in many cases, in no case has definite cure resulted, or the blood picture of pernicious anemia been fundamentally changed.

¹ Ztschr. f. Hyg., 1910, xvii, 189.

² Centralblatt f. Bak., 1913, Ixviii, 292.

³ Jour. Amer. Med. Assoc., December, 1913.

diagnosed microscopically. The majority of the cases show the glands to be of the endothelioid type described by Reed and Longcope. They report favorable vaccine results in some of the cases, practically all of which were simultaneously treated with the Roentgen-ray. This agent, as is well known, often causes decrease in the size of the cervical glands, but as a sequel to this treatment the thoracic and retroperitoneal nodes seem to develop faster.

Since every case of this disease that reacts favorably or unfavorably to an autogenous vaccine is of value, I feel justified in reporting this single case, even though my vaccine results are distinctly unfavorable:

The patient under consideration was a male, aged fifty-seven years. He had worked as a carpenter all his life. He was first seen May 8, 1915, and gave the following history: About one year ago he noticed a stiffness in the back of his neck which could never be made to disappear completely, and which was aggravated by slight chilling. Three months later he noticed a gland under the right tonsil somewhat enlarged, and accidentally discovered two small kernels in the occipital region. In February, 1914, other glands appeared on the right side of the neck, with a beginning involvement in a similar location on the opposite side. They had all been of rapid growth, were painless, and were freely movable under the skin. The tonsils were not greatly enlarged, and no history of repeated tonsillitis or sore throat was obtainable. The Wassermann reaction, urinalysis, and von Pirquet test were negative. The blood findings were as follows: reds, 4,900,000; whites, 10,200; hemoglobin, 89 per cent. A differential count of 500 cells shows: polymorphonuclears and transitionals, 62 per cent.; lymphocytes, 20 per cent.; large mononuclears, 14 per cent.; eosinophiles, 4 per cent.; no myelocytes or basophiles. No pathological changes in the red cells.

May 8, 1914, a lymphatic gland, with capsule intact, was removed from the right submaxillary region under local anesthesia. This will be known as R I. It measured $2 \times 3\frac{1}{2}$ cm., and had been growing for about three months, attaining most of its size in the last month.

On the left side the most recently involved gland was removed. It was located at the level of the cricoid cartilage under the sternomastoid. An incision was made in this muscle, and under moderate pressure from the forceps this gland, which was decapsulated, accommodatingly popped up through the incision. Its size was 1×2 cm. It was transferred directly to a tube of whole blood glucose agar. It will be known as L I. There was also removed from the same location a circular node recently involved, and about 6 mm. in diameter. It will be known as L II.

A pathological examination of the glands showed the following changes: For the most part the histological architecture of the

gland was destroyed. There was marked lymphoid hyperplasia in addition to a striking hyperplasia of the endothelial cells lining the lymph sinuses. A few multinucleated bizarre-shaped endothelioid giant cells were present, but no eosinophiles were observed. A diffuse sclerosis was just beginning. In some parts of the early nodes the arrangement of the gland had not been disturbed, and the proliferation of the endothelial cells lining the sinuses gave the appearance of densely packed cords of cells. In other areas only the lymphoid hyperplasia was noticeable.

Gland R I was washed in sterile normal salt solution and transferred to a sterile Petri dish. It was longitudinally incised and divided into three parts. The following disposition was made of the sections: A suitable portion was placed in formalin for pathological examination, the result of which has just been described. A second portion was placed in a sterile mortar and ground in sterile air. An emulsion was made in sterile normal salt solution and was planted on fifteen tubes of different kinds of media. The results of these cultural findings are not detailed in this article because they were the same in substance as were derived from the third portion of the gland, the results of which are detailed in the protocol. This portion was cut into small pieces and planted on several tubes of the following kinds of media: (1) 2 per cent. glucose agar, plus 10 per cent. beef serum; (2) 2 per cent. glucose bouillon plus 10 per cent. beef serum; (3) 2 per cent. glucose agar plus 5 per cent. whole human blood; (4) 2 per cent. glucose bouillon plus 10 per cent. ascitic fluid; (5) 2 per cent. glucose agar plus 5 per cent. whole human blood, about three weeks old. These media were incubated forty-eight hours before their use in these experiments. For the sake of convenience and brevity these different varieties will be referred to as Media 1, Media 2, etc., in the protocols.

An examination of the protocols of the cultural results discloses several things of interest: The marked pleomorphism of the organism has been mentioned by Bunting and Yates, and it is indeed one of its striking as well as its confusing features. Some of the diphtheroids are very large, these usually being club forms or ones heavily barred. Others are short and thick, corresponding to the solid type of the diphtheria bacillus. Under certain conditions the coccoid forms of varying size and staining power are developed. Branching forms were not uncommon. Some have a long, terminal filament, usually wavy in character. This may branch, or it may give rise to a more or less complex network which when stained by Gram's method is easily decolorized. Many of the coccoids have shorter spicules or projections of this character, while the wavy, pale filaments may also be seen free in the smears, and which show the above-mentioned characteristics. All these forms usually disappear in the transplants. The filaments are interesting in rela-

tion to the supposed spirochetes seen by Proescher and White⁴ in Hodgkin's glands, and thought by them to be the etiological factor in the disease. Their observations have not been generally confirmed. These filaments may also throw light on the origin of the spirochetes of Vincent's angina. They have never been cultivated, and are supposed by Tunnicliffe⁵ to be outgrowths of the fusiform bacillus of this condition. They can usually be seen as thin, wavy filaments attached to one end of the bacillus in a well-stained preparation.

There was considerable variation in the gross features of the cultures. On blood-agar the growth began, as a rule, in the water of condensation. It grew slowly on the slant, appearing for the most part as a moist dewdrop formation, thus resembling the *Streptococcus pyogenes*. Later it turned a light gray color and grew more luxuriantly. It had a decided preference for a moist surface. It would lie dormant for some time on the surface of a dry medium, but would grow readily when a little distilled water or sterile salt solution was added to the medium. Not infrequently the individual transplanted colonies would become opaque with unequal intensity, giving the colony a stippled appearance. On beef serum and plain glucose agar the growth was slow and sparse, but became more luxuriant with frequent transplants. The cultures gradually became chromogenic, producing first a yellow and later an orange or pink pigment. One culture transplanted May 26, 1914, in gelatin was viable December 1, having developed an orange pigment. The bacillus was decidedly aerobic, spreading arborescently over the surface of the gelatin in sunflower fashion, while the beaded growth along the stab had not perceptibly progressed. The viability was best preserved on gelatin.

Bouillon was diffusely clouded during the first few hours of growth, but soon cleared up, giving rise to a moderate quantity of fine granular sediment, collecting along the sides and on the bottom of the tube. When beef serum was added to the glucose bouillon the tendency for the organisms to clump was quite noticeable.

Neither glucose nor lactose was fermented, nor was a trace of acid produced even when using such a delicate indicator as Andrade's reagent⁶ (decolorized acid-fuchsin).

The organism was resistant to antiformin and was non-acid fast. It stained faintly in Loeffler's, but easily with gentian violet and carbolfuchsin. The best differentiation was brought about by the method of Gram, to which it reacted strongly under favorable conditions. But any change of environment had a remarkable effect on its power to retain this stain.

⁴ Münch. med. Wehnschr., 1907, liv, 1868; Jour. Amer. Med. Assoc., 1907, xlix, 1115.

⁵ Jour. of Infect. Dis., 1906, iii.

⁶ Annual Report United States Marine Hospital Service, 1895, p. 385.

In general it can be said that the growth on old blood agar and on dry media caused a large number of the organisms to be decolorized. In the condensation water of cultures a week old such changes could easily be seen. In some cultures all grades of reaction to this stain might be seen; in others, the entire culture was finally decolorized. Prolonged growth on the simple media was also favorable for the retention of this stain. However, when the coccoid bodies were developed by any of these processes they were much more constant in their positive reaction to the Gram stain than were the bacilli. The reasons for these deductions can be seen by consulting the protocol.

- May 15, 1914. L I.
- May 14, 1914. Transplant 2.
- May 21, 1914. Transplant 11.
- May 15, 1914. L I, both slant and water of condensation.
- May 15, 1914. Transplant 19, L I.
- May 16, 1914. Transplant 26, L I.
- May 13, 1914. Transplant 8, L II.
- May 22, 1914. Transplant 31, L I, condensation water.

Another point of interest toward which attention was directed, lay in determining whether the cocci or coccoid forms were derived from the bacilli or represented a separate bacterium. By first shaking up the organisms with sand, and then plating them out by the dilution streak method, isolated colonies containing no coccoids were found. When transplanted under unfavorable conditions, an abundance of these forms appeared. (See plate cultures I, II, and III, under subcultures of gland L I.) In addition it will be seen that gland L I and L II contained none of these when the growth first started. By following the examinations of the condensation water of L I from day to day a progressive shortening of the organism was seen, until finally many of these anomalous forms appeared. One tube of gland L II which had contained no coccoids, ran along for several days without change, either macroscopically or microscopically. Then from May 15 to May 16 the growth suddenly changed from a transparent dewdrop character, to a more luxuriant opaque formation. Microscopically, practically nothing but coccoids were found. (See L II, May 16.) Other reference to protocols bearing on this point are transplants No. 3, May 12 and May 14; transplant No. 16 of May 14; transplants Nos. 14 and 15, of May 18.

It seems probable that the coccoids represent involution forms of the bacillus, as they flourish under an unfavorable environment. If, for example, the organism grows on a medium which delays its appearance, or on a stale or dry medium, coccoids appear quickly. The age of the cultures also has a decided bearing, especially if it be on one which degenerates rather rapidly, *e. g.*, blood agar. (Under L I protocol, see description under date of May 13

and May 15 (Plate I). Transplant II of May 21, 1914; transplant 19 of May 15, 1914; transplant 25; transplant 35 tube (3) of L I, May 18, 1914; under L II see transplant 8, and under R I see tube number 5, May 15, 1914; transplant 9 of May 12, 1914.

Attempts to have the coccoids develop in chains failed. (Transplants 40 and 41.) No true spore formation or motility was observed. Gelatin was not liquefied, but was the best medium among those I used to preserve the viability. Large involution spherical forms were present in old cultures of this medium, which were usually chromogenic.

No attempt was made to enter into all the details of morphology, and the cultural and biochemical characteristics which go to determine unequivocally the location of the organism in its proper place. Only those were entered into which would suffice reasonably for its identification as described by those who first isolated it. However, the apparently rare filamentous forms and its chromogenic capacity were novel to me.

PATHOGENICITY. May 18, 1914, a guinea-pig and a rabbit were each injected with a salt suspension of 1 c.c. of the bacillus from the right gland into each thigh subcutaneously. A rabbit and a guinea-pig were also treated with 1 c.c. of the suspension from the left gland. This time the injection was made subcutaneously into the right thigh, and also intraperitoneally, 1 c.c. being given in each place.

None of the animals showed symptoms, but the rabbit which received the injections in two locations soon lost the extreme vivacity which had characterized her heretofore. Progressive diminution in weight and strength occurred until October 20, 1914, at 5 P.M., when the animal died in an extremely emaciated condition. (Original weight, 1940 grams; antemortem weight, 860 grams.) No rise in temperature was observed at any time.

Autopsy, October 20, at 6 P.M. Smears were made from all organs, but were negative. Parts of the lung, liver, heart, kidneys, spleen, and ovaries were placed in formalin and subjected later to a pathological examination, which was negative. Lymphatic involvement was also negative. Parts of the organs were planted on blood agar. Results were negative except with an ovary, which after five days yielded on the slant two small gray colonies, which proved to be diphtheroids of the same character morphologically as the ones injected. The condensation water surrounding the tissue was rich in the same organism.

On transplants to blood agar the organism grew in light gray colonies after forty-eight hours. It was a strongly Gram-positive, non-acid-fast diphtheroid. It produced no acid on glucose and did not liquefy gelatin. It was decidedly pleomorphic, following the same general lines as its supposed antecedent, except that no coccoid forms have been observed up to this time.

Cultures of it have been injected daily into rabbits for a month, but so far the animals have shown no significant signs. Animal experiments with both organisms are being continued.

VACCINE TREATMENT AND SUBSEQUENT HISTORY. Vaccines were prepared from the bacilli of both glands and from the coccoid forms of the left gland cultures. The organism was grown forty-eight hours on glucose-agar, washed down in normal salt solution, filtered through glass-wool-cotton filter to remove clumps, heated to 56° for one hour, after which 0.1 formalin was added. Controlled for four days on blood agar.

May 25, at 11 A.M., five millions of the killed bacilli of gland L I were given subcutaneously into the left arm. No temperature; no local, focal, or constitutional reaction.

May 28, ten million bacilli given in the same manner. Glands of right side given a mild Roentgen-ray treatment. No reaction of any sort.

May 30. Some improvement. He turned his head more easily; all palpable glands receded slightly and the patient felt generally improved.

May 31. At 8 A.M., fifteen millions of the dead organisms from L I were given. No reaction of any kind. No improvement in his condition. In fact, the glands in the cervical region were gradually enlarging and the axillary glands on the right side, and the inguinal glands on both sides were involved. A Roentgen-ray treatment given, but no improvement resulted.

June 8. A vaccine of 25,000,000 given subcutaneously. He returned home until July 13. During this time he received three doses of vaccine, the sizes of which were 50,000,000, 75,000,000, and 85,000,000. He was not under my control at this time, but was treated by his home doctor. He reported no improvement from any of the vaccines. The dose of 85,000,000 produced a rise in temperature of 3°, which receded in forty-eight hours. The glands continued to enlarge.

July 13. I administered a dose of 150,000,000. He had only a slight temperature rise, but his condition did not change.

He did not return for further treatment, but went to Chicago some time later, where he was treated by Dr. E. C. Rosenow. From him I learned that an axillary gland had been removed and a vaccine prepared. I next heard from his home town that he died about September 1.

In this case I am unable to see any good results whatever that can possibly be traced to his autogenous vaccine, although the dosage did not go above 150,000,000. Excepting a few transitory improvements, which might be traced to the Roentgen-ray, his downward course was a rapid and uninterrupted one from May 8 until July 13, and his demise six weeks later would seem to conform to the previous rapidity with which the disease pro-

gressed. I might add that the removal of the glands by surgical operation caused a rapid enlargement of the neighboring glands. I can only hope that my case was atypical and that the general run of the cases will yield to treatment.

PROTOCOL OF CULTURAL RESULTS.

Media No. 1—Two per cent. glucose agar plus 10 per cent. beef serum. May 9, 1914: No growth. May 10, 1914. No growth. May 11, 1914: No growth.

Media No. 2—Two per cent. glucose bouillon plus 10 per cent. beef serum. May 9, 1914: No growth. May 10, 1914: The bouillon is diffusely clouded. Microscopically bacilli of varying size and shape are found. Many solid and barred types, while a few have bipolar granules. A few coccoid forms are present. Stain well with Gram but faintly with Loeffler's. May 11, 1914: A heavy white precipitate is deposited at the bottom of the tube, while the supernatant fluid is clear. No change microscopically.

Media No. 3—Two per cent. glucose agar plus 5 per cent. whole human blood. May 9, 1914: Negative. May 10, 1914: Negative. May 11, 1914: Negative.

Media No. 4—Two per cent. glucose bouillon plus 10 per cent. ascitic fluid. May 9, 1914: Negative. May 10, 1914: Negative. May 11, 1914: Negative.

Media No. 5—Two per cent. glucose agar plus 5 per cent. whole human blood (three weeks old). May 9, 1914: Negative. May 10, 1914: Negative. May 11, 1914: Negative.

Left Gland L I.

Media No. 1—Two per cent. glucose agar plus 10 per cent. beef serum. May 9, 1914: Negative. May 10, 1914: Negative. May 11, 1914: Negative.

Media No. 3—Two per cent. glucose agar plus 5 whole human blood. May 9, 1914: Negative. May 10, 1914: Negative. May 11, 1914: Negative.

Media No. 5—Two per cent. glucose agar plus 5 per cent. whole human blood (three weeks old). May 9, 1914: Negative. May 10, 1914: The cloudy fluid surrounding the piece of gland shows the same findings as occur in the bouillon from the right gland, except no coccoid forms are present. Gram-positive. May 11, 1914: Increase of turbidity in the condensation water. This was permitted to run over the slant of agar. See transplants 2, 10, 11, 19, 22, 23, 25, 26, 31, 32, 33, 35, 40, 41, 42 under protocol of subcultures, L I.

Left Gland L II.

Media No. 3—Two per cent. glucose agar plus 5 per cent. whole human blood. May 9, 1914: Negative. May 10, 1914: Negative. May 11, 1914: Negative.

Gland R I.

Media No. 1—May 12, 1914: No growth. May 13, 1914: Growth appeared for first time. Many coccoid forms. Variation in reaction to Gram stain. May 14, 1914: No change.

Media No. 2—May 12, 1914: Increase of growth. No change microscopically. See transplants 1, 3, 4, 6, 7, 9, 16, 17, and 29 under Protocol of subcultures R I. May 13, 1914: No change. May 14, 1914: No change.

Media No. 3—May 12, 1914: Negative. May 13, 1914: Negative. May 14, 1914: First growth appears. Dewdrop formation. Diphtheroid and coccoid forms. Gram positive.

Media No. 4—May 12, 1914: Negative. May 13, 1914: Negative. May 14, 1914: Negative.

Media No. 5—May 12, 1914: First growth shows fine barred and solid bacilli. Gram positive. May 13, 1914: Growth first occurred as Gram positive bacilli and coccoids. May 14, 1914: Many barred forms.

Gland L I.

Media No. 1—May 12, 1914: Negative. May 13, 1914: Negative. May 14, 1914: Negative.

Media No. 3—May 12, 1914: Tube 41 shows fine, slender, long bacilli and coccoid forms. All are Gram positive. May 13, 1914: The slant shows many coccoids. Marked pleomorphism. The condensation water shows bacilli, narrower and shorter, but maintaining the granulation. Sparsity of coccoids. May 14, 1914: No change.

Media No. 5—May 12, 1914: The slant shows a thin, grayish, slimy growth. Microscopically, diphtheroid bacteria of great diversity of size and shape. Clubs, dumb-bells, and grotesque forms. Practically all have one or more deep blue granules located at the dilated end of the bacillus. Metachromism. Loeffler's stain negative, organisms are strongly Gram positive. May 13, 1914: Tube 2, L I. All coccoid bodies. Occur singly as diplococci, or in groups. Great diversity in staining power. This is first growth on Tube 2, L I. May 14, 1914: No growth as yet on slant. Turned condensation water over slant.

Left Gland L II.

Media No. 3—May 12, 1914: Negative. May 13, 1914: All bacilli as in Tube 1, L I. Dewdrop colonies on slant. See transplants 8, 13, 14, 15, 28, 30, 34, and 38. May 14, 1914: No change.

Gland R I.

Media No. 1—May 15, 1914: No change. May 16, 1914: All are Gram-positive coccoids.

Media No. 2—May 15, 1914: No change. May 16, 1914: No change. May 21, 1914: Most of the bacilli are Gram-negative. Some Gram-positive coccoids found.

Media No. 3—May 15, 1914: Many barred forms. Positive to Gram. May 16, 1914: No change.

Media No. 4—May 15, 1914: Negative. May 16, 1914: No growth occurred.

Media No. 5—May 15, 1914: No change. May 16, 1914: No change.

Gland L I.

Media No. 1—May 15, 1914: Negative. May 16, 1914: No growth occurred.

Media No. 3—May 15, 1914: Condensation water shows many Gram-positive coccoids, and many Gram-negative diphtheroid bacilli. May 16, 1914: Condensation water of L I contained small Gram-positive, barred bacilli.

Media No. 5—May 15, 1914: Fine dewdrop growth, just starting to turn gray. Strongly Gram-positive cocci. May 16, 1914: No change.

Gland L II.

Media No. 3—May 15, 1914: Forms are shorter and more of the solid type, but still bacilli. May 16, 1914: All Gram-positive cocci. The slant is no longer of dewdrop appearance, but is light gray.

PROTOCOL OF SUBCULTURES OF GLAND REMOVED FROM THE RIGHT
CERVICAL REGION (R I).

First generation of subcultures.

May 12, 1914—Transplants 1 and 3 planted May 11. From Media No. 2 to fresh whole blood agar (Media No. 3). Both tubes show some heavy gray colonies and some that look like dewdrops. The former are Gram-positive, slender, long bacilli with marked granulations. Only a few club forms. Barred type predominates if the media is a little old or dry. The dewdrop colonies show the same bacteria.

May 17, 1914—Transplants: 6 and 7 from Media No. 2 to Media No. 1. Shows a pure culture of very large bacilli with most intense barring. No coccoid forms present. Protoplasm is light blue, but the bars are intense blue. Transplant 29 is from the incubated

gland in the Petri dish on which colonies appeared first May 12. Planted on beef serum bouillon. A precipitate formed in the bottom of the tube. Supernatant fluid clear. No clumping. Shows Gram-positive coccoid forms.

May 15, 1914—Tube 5. First appearance of growth May 12. Single colony growing from a piece of gland tissue. Colony gray and has not spread laterally as much as in depth. Microscopically, short, fat Gram-positive bacilli of the solid type, as well as thinner curved Gram-negative filaments, which may or may not be bacteria.

Second generation of subcultures.

May 13, 1914—Transplant 4 from dewdrop colonies of transplant 1 to Media No. 2. Shows slender solid type bacilli. Gram-positive.

May 16, 1914—Transplant 9 from dewdrop colonies of transplant 1 to Media No. 5. Many coccoid forms mixed with slender bacilli. Variation in reaction to Gram stain. Some bacilli are greatly decolorized.

May 14, 1914—Transplant 16 from transplant 3 to Media No. 5. Shows Gram-positive barred and coccoid forms. Transplant 17 from transplant 6 to Media No. 1. Shows same forms as transplant 6. Transplant 18 from transplant 1 to Media No. 3. Dewdrop colonies. Microscopically, strongly Gram-positive, barred bacillus.

Part of right gland in Petri dish incubated at 37°, May 8. Small gray colonies appeared May 12. Mostly they are Gram-negative cocci, although a few are Gram-positive. Some colonies are very fine, slender bacilli, with coccoid forms which are Gram-negative.

Subsequent examination of previous subcultures.

May 13, 1914—Transplant 3. Still shows slender, long bacilli. Gray growth gradually becoming opaque.

May 14, 1914—Transplant 3 shows true coccoid forms, but little else. The individuals are quite large. There are many short, plump bacilli and some barred types. Compare description of same culture of May 12.

May 14, 1914—Transplant 6. No change. All Gram-positive.

May 16, 1914—Transplant 6. Very few are Gram-positive. Mostly Gram-negative, barred forms.

May 13, 1914—Transplant 1. Growth changed from dewdrop to gray, and colonies are opaquely stippled.

May 21, 1914—Tube 5, R I, transplanted to beef serum. Very slow development. Fusiform and barred types. Only moderately positive to Gram.

May 21, 1914—Transplant 17. Large, barred bacilli. Some positive and some negative to Gram.

First generation on different media.

May 12, 1914—Transplant 2 from condensation water of L I on Media No. 3 to Media No. 3. An apparently pure culture of a bacillus, uniform in size and shape, with many Gram-positive, barred forms. Transplant 10 from the condensation water of L I to beef serum. (Media No. 1.) Many barred forms and some coccoids.

May 21, 1914—Transplant 11 from L I, May 13, to old blood agar. All are cocci of varying sizes. Some Gram-positive and some Gram-negative.

May 15, 1914—Transplant 19 planted May 14, 1914, from slant of L I to Media No. 5. Shows a fine dewdrop growth. Microscopically, shows coccoids, moderately Gram-positive.

May 16, 1914—Transplant 25 from agar slant L II on Media No. 3 to Media No. 1. Mainly small Gram-positive cocci, and a few bipolar bacilli.

May 17, 1914—Plate I. May 11, 1914, a dilution streak on Petri dish of Media No. 5 from condensation water of L I. No growth until plate was moistened with salt solution. Then the individual colonies appeared along the streak. An examination of individual colonies shows Gram-positive and Gram-negative diphtheroids in the same colony.

May 18, 1914—Plate III from condensation water of L I to Media No. 3, planted May 16. Same results as on Plate 1.

May 18, 1914—Transplant 35 from condensation water of L I, planted May 12, 1914 on Media No. 5. First growth May 17, 1914. Nothing but Gram-positive coccoids.

May 18, 1914—Transplant 31. Entire gland L I transplanted to Media No. 3 on May 16, 1914. Shows diphtheroids of remarkable diversity of form. They are strongly Gram-positive. Many drum-stick forms are present, the stems of which are projected into long tails which stain Gram-negative. Sometimes these whips or tails branch simply, but at other times the arborization is almost dendritic. These Gram-negative filaments are also free in the smear. They may explain the apparent Gram-negative filaments or bacteria found in the other cultures. The oval coccoids often have tails at both ends. Some are Gram-positive and others Gram-negative. They resemble early Leishmann-Donovan bodies. Transplant 35. From condensation water of L I, planted May 12 on Media No. 5. Nothing but Gram-positive coccoids.

Second generation on different media.

May 16, 1914—Transplant 26, from transplant 23 to Media No. 3. Diphtheroids and coccoids which show all grades of reaction to Gram stain.

May 18, 1914—Transplants 32 and 33 from transplant 26 on Media No. 3. About same forms as described under transplant 31, excepting there are fewer coccoids and Gram-negative filaments.

May 18, 1914—Transplant Plate II. Transferred a colony of diphtheroids from Plate I to a plate of Media No. 1. Microscopically, they are all Gram-positive cocci of varying sizes. There are some bipolar bacilli, the bodies of which stain poorly with Gram.

May 18, 1914—Transplant No. 2, transplanted to Media No. 3 from original colonies of Plate I which were cocci. Microscopically nothing but Gram-positive cocci. Transplant No. 10 is from Plate III into human serum bouillon. In eighteen hours, growth shows cocci, but merely a suggestion of chain arrangement. Nothing definite. Transplant 41 from Plate III into beef serum bouillon. A very decided clumping of the cocci occurs. No suggestion of chain arrangement.

Subsequent examinations of subcultures L I.

May 13, 1914—Transplant 2. Slender, barred bacilli in the condensation water. No change.

May 14, 1914—Transplant 2. Great variation in the reaction to Gram-stain. Many bacteria are nearly decolorized.

May 22, 1914—Transplant 31. The slant shows many branching forms of diphtheroids. Gram-positive. The shapes are more regular in the condensation water, and do not hold the Gram-stain well.

May 18, 1914—L II, tube 3, planted May 8. First growth May 15. Almost all Gram-positive cocci. Very few diphtheroids.

Subsequent examinations of subcultures L II.

May 21, 1914—L II on Media No. 2. No change. All Gram-positive coccoids.

PROTOCOL OF SUBCULTURE OF THE SECOND GLAND REMOVED FROM THE LEFT CERVICAL REGION (L II).

First generation of different media.

May 13, 1914—Transplant 8 from L II Media No. 3 to Media No. 1. Short plump forms with small amount of barring and granulation. They are not Gram-negative, but are greatly decolorized.

May 17, 1914—Transplant 28 is from slant of gland L II into Media No. 2. Precipitate in the bottom of the tube, while the supernatant fluid is clear. Shaking yields a finely granular cloud. Marked clumping tendency. Transplant 30 is from L II slant into human serum bouillon. Same findings as transplant 28.

May 18, 1914—Transplant 34. L II planted on Media No. 1, May 15. Shows Gram-positive cocci. Transplant 38, from tube 2, gland L II which showed nothing but cocci on first examination. No change in this transplant.

May 18, 1914—Transplant 13, from transplant 28 to Media No. 1. All Gram-positive cocci. Transplant 14 and 15 are from transplant 28 to Media No. 5. Small Gram-positive coccoids. Some do not hold the stain well.

THE DIAGNOSIS BETWEEN PRIMARY AND SECONDARY ACUTE CARDIAC PICTURES.¹

BY ROBERT N. WILLSON, M.D.,

PHILADELPHIA.

It is with a full appreciation of the intimacy of the confidence imposed upon the consultant, and of the restrictions limiting the ownership of clinical data acquired under the relations of professional privilege and friendship, that I am venturing to sketch in barest outline four cases seen recently in conference with medical friends.

The first was of a man who complained of intense dyspnea on the slightest exertion in bed, of substernal oppression, of palpitation, and of sharp precordial pain. The pulse was feeble, slightly irregular, and in rate 120. The temperature was subnormal. The cardiac symptoms had impressed his physician to the extent of leading him to minimize the fact that the patient was breathing little, if at all, with his left side, which posteriorly showed unmistakable evidence of a bronchopneumonia, from which in due course he died.

The second patient was a young woman whose pulse rate, when I first saw her, was 130 and above on the slightest exertion. Even at rest it remained constantly about 110. She had been an excessive tea and coffee drinker, and had been in the habit of frequently using headache powders. She was of a highstrung, neurotic temperament, and the victim of long indoor hours, overworry, and work. When sent to me for examination she could hardly walk from the door to a chair. Palpitation and dyspnea were distressing, and were even worse when at rest in bed than when exercising. Moderate numbness and pain at times extended down the right arm. There was no cough, no sputum, no hemoptysis. She had

¹ Read before the Section on Medicine, College of Physicians of Philadelphia, November 23, 1914.